EXHIBIT F

83 0759

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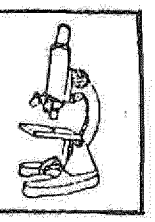

SOMERVILLE, NEW JERSEY 08876

To: Dr. A. Lunn

March 23, 1983

cc: Mr. E. A. Block
Dr. A. W. Fetter
Dr. A. J. Levy
to
Dr. R. L. Kronenthal
Mr. R. Lilenfeld
Dr. D. C. Marshall
Dr. A. Melveger
Dr. W. D. Sheffield
RDCF

Subject: PROLENE* (POLYPROPYLENE) MICROCRACKS

Tony,

Since the latest "human retrieval" specimens of PROLENE suture showed surface microcracking (ERF Acc. No. 83-165), I thought it would be useful to review the histological preparations from past samples more critically. The slides were reviewed by light microscopy using polarized light to help identify the cracking. The results are listed below.

ERF Accession No.	PROLENE Suture Size	Site	In Vivo Residence	Fixative	Findings
70-148	not identified	abdomen	3-5 years	formalin	no cracking noted
79-220	Sample 1A 5/0	vascular graft	6 years	formalin	cracking evident
	Sample 2 5/0	vascular graft	2.5 years	formalin	no cracking noted
79-320	5/0	vascular graft	4.5 years	formalin	cracking evident
81-266	3/0, 4/0 or 5/0	vascular graft	7.5 years	formalin	no cracking noted

Attached are photographs of samples from ERF Acc. No. 79-220 and 79-320. The original 35mm slides are available. If you felt it appropriate, I'd be happy to show these at the next PROLENE Microcrack Committee meeting.

Barbara
B. Matlaga

799A/drp

Attachments

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79-320 SECTION F S/O PROLENE X270 4.5 YEARS

79-320 SAMPLE 1-A S/O PROLENE X270 6 YEARS

79-320 SECTION F S/O PROLENE X270 POLARIZED LIGHT 4.5 YEARS

79-320 SAMPLE 1-A S/O PROLENE X270 POLARIZED LIGHT 6YRS

83 0783

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ETHICON
RESEARCH
FOUNDATION
SOMERVILLE, NEW JERSEY 08876

To: Mr. P. Marshall

March 29, 1983

cc: Mr. E. A. Block
Mr. G. G. Jones
Dr. A. J. Levy
to
Dr. R. L. Kronenthal
to
Dr. T. S. Graves
Dr. D. C. Marshall
Dr. A. Melveger
Dr. A. Lunn
Mr. H. L. Schrayer
to
Mr. B. O'Holla
RDCF

Subject: HUMAN RETRIEVAL SPECIMENS FROM DR. ROGER GREGORY, NORFOLK SURGICAL GROUP

ERF ACCESSION NO.

83-165

PROJECT NO. 47201

SUMMARY

Formalin fixed tissue samples containing Dacron graft material and PROLENE* (polypropylene) sutures were submitted for evaluation from the Norfolk surgical group. Sample #1 was resected from a false aneurysm from a patient six years after an aorto-bifemoral graft was inserted using 6-0 PROLENE suture. Sample 2 was resected 5.5 years after an aorto-femoral bypass graft was inserted using 5-0 PROLENE suture.

Segments of 5-0 PROLENE from specimen #2 were carefully removed from the graft and tested for breaking strength evaluation (BSE). Results were 54% breaking strength remaining when measured against a similar size control. No segments of an adequate length were recovered from sample #1 to be tested for breaking strength. PROLENE sutures from both samples displayed surface cracking when examined by light microscopy.

Histological examination revealed a cellular response consistent with other long-term implants of Dacron graft. The reaction surrounding the PROLENE suture was minimal in all cases.

Reported by Barbara Matlaga 3/18/83
B. Matlaga

Approved by W. D. Sheffield 3/21/83
W. D. Sheffield, V.M.D., Ph.D.

Approved by A. W. Fetter 3/21/83
A. W. Fetter, D.V.M., Ph.D.

455E/drp

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SAMPLE #1

Description

A fixed tissue specimen measuring approximately 1.5cm x 0.8cm was received for examination. Grossly, tissue was adherent to only one side of the specimen, Figure 1. On the fabric side of the specimen, a knot and running suture line was visible, Figure 2. This specimen was resected from a false aneurysm 6 years after an aorto-bifemoral graft was inserted using 6-0 PROLENE sutures. (See attached memo Gregory to Marshall, patient Miriam Brown, 2/4/83).

Suture Evaluation

Three suture segments were carefully removed from the tissue specimen. These measured approximately .08cm, 1.2cm and 3cm (with knot), respectively. These specimens were considered too short for breaking strength evaluation. The diameters of the sutures were between .080mm to .070mm which is consistent with USP standards for a nonabsorbable 6-0 suture. Light microscopic evaluation of these strands revealed surface cracking, Figure 3.

Histological Evaluation

The histological observations of the sections revealed the presence of Dacron graft fibers infiltrated by macrophages, giant cells and fibroblasts. An acellular eosinophilic material was also seen surrounding the graft fibers. Adjacent to the graft segment was a thick capsule of well-vascularized connective tissue. Cracking of the suture surface was also evident in a longitudinal section of PROLENE located near the graft fibers, Figure 4. The cracking appeared along only one edge of the PROLENE and was especially prominent when viewed with polarized light, Figure 5.

SAMPLE #2

Description

A fixed tissue specimen measuring 3cm x 3cm was received for examination. Grossly, a segment of Dacron measuring 1.3cm was firmly adherent to the tissue mass and a PROLENE suture line was evident, Figure 6. This specimen was resected 5.5 years after an aorto-femoral bypass graft was inserted using 5-0 PROLENE suture. (See attached memo Gregory to Marshall, patient Paul Newman, 2/4/83). Another segment of PROLENE was free-floating in the fixative container and presumably was removed from this graft.

Suture Evaluation

One length of suture, with a knot, was carefully removed from the tissue specimen. The legs measured 1cm and 2.5cm, respectively. The free length of suture measured 8.2cm and had areas of kinks and instrument damage on the surface, Figure 7. The diameter of the strands were .145mm which is consistent with USP standards for a 5-0 nonabsorbable suture. A 4cm segment from the long strand, which was relatively free from instrument damage, was used for breaking strength evaluation. Measured against a 5-0 PROLENE

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control, this segment had 54% strength remaining. Light microscopic evaluation of this strand revealed surface cracking identical to Sample #1, Figure 8.

Histological Evaluation

The histological observations of this tissue revealed a row of Dacron graft fibers infiltrated with foreign body giant cells, macrophages and fibroblasts. An acellular eosinophilic fibrinoid material was located among the graft fibers in some areas. This fibrinoid material was in varying states of degredative change with focal areas of basophilia suggestive of early mineral deposition. Located adjacent to the graft were segments of dense fibrous connective tissue measuring approximately 1mm x 3mm. These areas may correspond to normal vascular tissue adjacent to the graft site. Remnants of internal elastic membrane were visible, based on an elastic tissue stained section, and the normal intima had evolved into a dense layer of collagen fibers. No endothelial cells were present on what was judged to be the luminal surface. Only one cross sectional profile of PROLENE was contained in this slide. No evidence of cracking was noted. The cellular response to the suture material was minimal.

CONCLUSION

The histological picture of the grafts in this study are consistent with other long-term human retrieval graft specimens we have evaluated in the past. This includes a foreign body response to the graft fibers along with a degraded acellular infiltrate. The tissue response to the PROLENE sutures was minimal in all cases.

Surface cracking was noted on the PROLENE sample from both explants. Why the cracking occurred or if this condition contributed to the loss of breaking strength (54%) could not be determined from this type of examination. It could also not be determined when or how the instrument damage occurred on the strand from Sample #2.

ETHICON

INC.

SOMERVILLE • NEW JERSEY

February 15, 1983

To: Mrs. B. Matlaga

cc: Mr. C. H. Fricke, III

Subject: EVALUATION REQUEST

Barbara, enclosed please find specimens of graft and suture material from two patients of Doctor Roger Gregory.

I would appreciate it if you could evaluate this material, and forward the results to my attention.

Thank you,

Paul R. Marshall

PRM:klk

Enclosures

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FEB 1 5 1983
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AND
SURGICAL ENDOSCOPY

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ROBERT E. McALPINE, M.D., RETIRED
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ROBERT G. GAYLE, M.D.

ADMINISTRATOR
DANIEL J. RODGERS, M.S.A.

February 4, 1983

Mr. Paul Marshall
Product Director, Cardiovascular Surgery
Ethicon, Inc.
Somerville, NJ 08876

Dear Mr. Marshall:

Enclosed for your evaluation is a speciman from a false aneurysm resected on 2/3/83. The patient is Miriam Brown. An Operative note from her original procedure is enclosed for your review of the suture material and graft involved.

I would be most interested in the status of the graft and suture material regarding tensile strength, etc.

Thank you for your help.

Sincerely,

Roger T. Gregory, M. D.

RTG:cg

DR. E. ROZAR
OP. NOTE
MIRIAM BROWN
577 66 01 32
1/4/77

CVU PVT

Gregory

PREOP DIAGNOSIS: AORTOILIAC DISEASE WITH BILATERAL SUPERFICIAL FEMORAL BLOCKS

POSTOP DIAGNOSIS: SAME

OPERATION: AORTO BY FEMORAL GRAFT WITH BILATERAL PROFUNDOPLASTIES

SURGEONS: DR. R. GREGORY
DR.E. ROZAR

ANESTHESIA: GENERAL ENDOTRACHEAL VIA DR. ASKEW

REPLACED: 3 UNITS OF PACKED CELLS AND 1 UNIT OF WHOLE BLOOD

PROCEDURE: This patient was placed in the supine position after satisfactory intravenous and arterial and EKG monitoring systems were connected to the patient. She was put to sleep under general endotracheal anesthesia. She was then prepped and draped from her nipples to her toes. A transverse skin incision was made and carried down to the skin and subcutaneous tissue and the anterior rectus sheath on both sides were excised. The rectus muscle bilaterally was then opened using bovie coagulation. The midline was then opened and cross clamped with Kellys and divided and ligated. The posterior rectus sheath, muscles and peritoneum were then opened using bovie. Exploration of the abdomen was then carried out. Appropriate retraction was done on the intestines moving all of the small gut up to the RUQ and the transverse colon above the midline. Retroperitoneum was then opened over the aorta. Small bleeders were clipped. The aorta was then exposed from just below the renal vein down to below the bifurcation. Proxixal and distal control were obtained, several lumbar arteries were clipped with hemoclips. It was decided at this time that we would indeed do an end to side anastomosis. The abdomen was then packed and both groins were opened, down to the artery and the common femoral, superficial femoral and profunda artery and its branches were all isolated using the vascular tapes. Tunnels were then placed just above the artery into the abdomen and kept open with Penrose drains. At this time the graft was brought up, blood was drawn from the aorta to preclot the graft. The graft was that of a 19 x 9 1/2 size. The aortic clamp was then clamped proximally and the hypergastric clamp was placed distally on the aorta and the aorta opened using an arteriotomy knife followed by Pott scissors. The graft was then brought up

Signed _____ M.D.

Name	Miriam Brown	Physician	Dr. E. Rozar
H. No.	577 66 01 32	Room	CVU
Date Dictated	1/4/77	Type of Report	Op Note
Date Transcribed	1/5/77 jlh	☒ NGH ☐ LMH	

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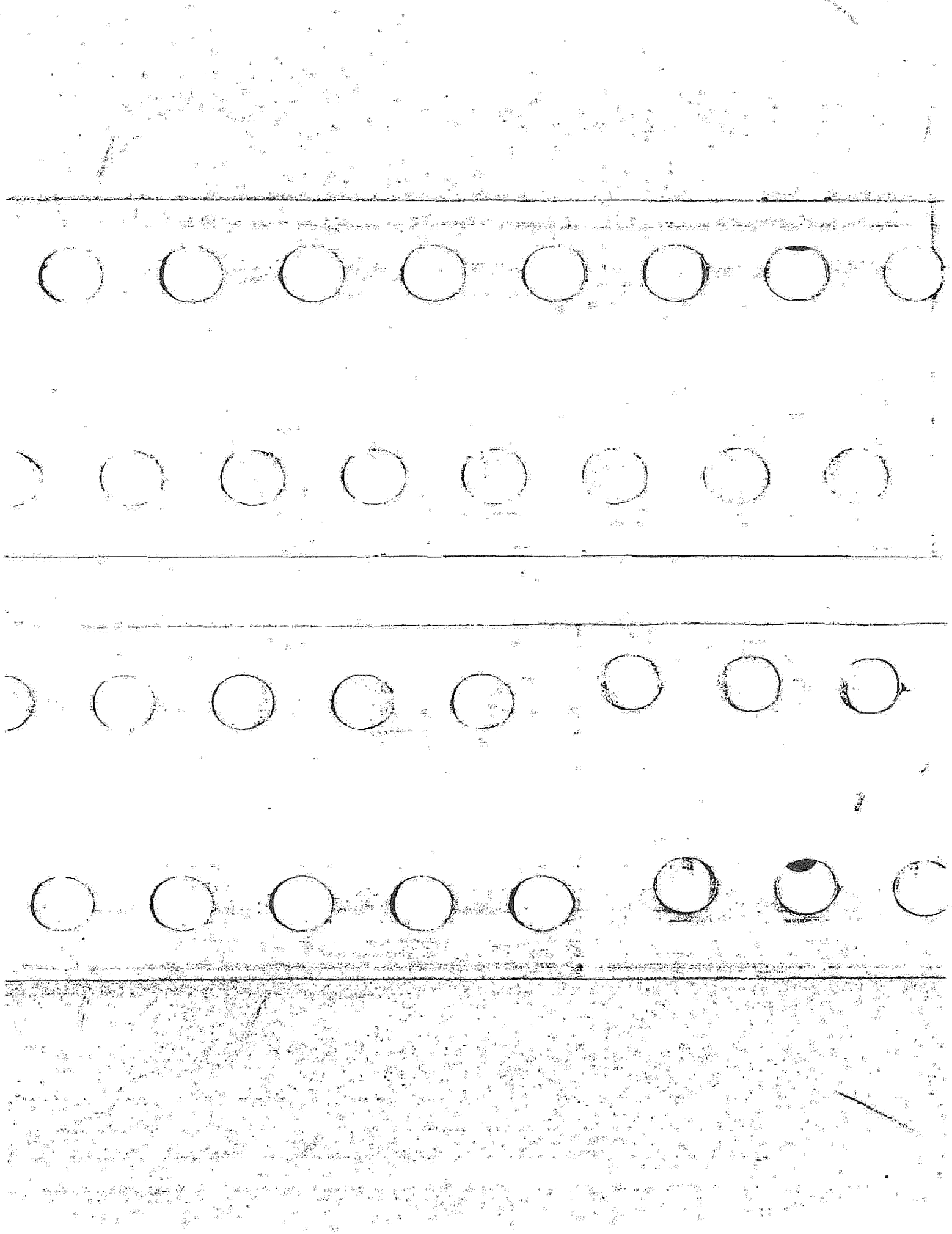

and using 3-0 Prolene, and end to side anastomosis was fashioned using running Prolene suture. Appropriate flushing maneuvers were done and the seal was good. The right limb of the graft was then brought through the tunnel. Appropriate vascular clamps were placed on the profunda superficial femoral and common femoral and an arteriotomy was done with a knife followed by Pott scissors and was opened up onto the profunda for a good ways to involve a profundoplasty. The right limb of the graft was then sewn to the common femoral and profunda using a running 6-0 Prolene suture. Appropriate flushing maneuvers were done when the anastomosis was completed, and then this was completed and the limb opened and there was no leaks. The graft clamp at this time, of course, had been placed on the l left limb of the graft. At this time, the left limb of the graft was placed through the tunnel and after appropriate vascular clamps were placed in the groin, an arterial line was done from the common femoral down into the profunda--in a like manner, the left limb of the graft was sewn to the common femoral and profunda using a continuous 6-0 Prolene suture. Appropriate flushing maneuvers were done and the anastomosis completed. There ws a good flow with the flow meter being placed on the graft on the left side showing 400 mls per minute and the right side, 340 mls. per minute. There was adequate hemostasis. Thrombin powder was inserted on both sides. Both groins were then closed using 2 layers of 3-0 Chromic followed by running and 3-0 Prolene to the skin. Exploration of the abdomen was then done again, and there was adequate hemostasis. The periaortic tissue was closed over the aorta, using interrupted 0 Chromic sutures. The peritoneum was then reapproximated to the form of the retroperitoneum by using a running 0 Chromic suture. The bowels were placed back in the abdomen and the posterior rectus sheath and peritoneum were then reapproximated using a running 0 Chromic suture. These were reinforced with interrupted 0 Ethiflex. The midline was reapproximated using 4 interrupted 0 Ethiflex sutures. The anterior rectus sheath and external oblique fascia and muscle were then reapproximated using a running #2 Tev Dek suture. The skin was then reapproximated using clips. A dressing was placed and the patient went to the Recovery Room in good condition. She had good hemodynamics, and both warm feet on leaving the Operative Suite.

Signed _____ M.D

Name	Miriam Brown	Physician	Dr. E. Rozar
H... No.	577 66 01 32	Room	CVU
Date Dictated	1/4/77	Type of Report	Op Note
Date Transcribed	1/5/77 jlh	☒ NGH ☐ LMH	

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STANLEY O. SNYDER, JR., M.D.
ROBERT G. GAYLE, M.D.

ADMINISTRATOR
DANIEL J. RODGERS, M.S.A.

February 4, 1983

Mr. Paul Marshall
Product Director, Cardiovascular Surgery
Ethicon, Inc.
Somerville, NJ 08876

Dear Mr. Marshall:

Enclosed is a speciman on a patient named Paul Newman, along with an operative report from the procedure performed many years ago when this was inserted. The sample is in Formalin and consists of dacron graft and suture material.

We would be most interested in the functional status of the suture material and graft which I believe would certainly be of mutual interest to both of us.

Sincerely,

Roger T. Gregory, M. D.

RTG:cg

OP
PAUL NEWMAN PVT
237 05 27 92
6/22/77 B6

SURGEON: J. WHEELER, M.D.
W. RIVERO, M.D.
B. FREEMAN, M.D.

PREOPERATIVE DIAGNOSIS: GENERALIZED ARTERIOSCLEROSIS, WITH OBSTRUCTION OF THE LEFT ILEAC ARTERY

POSTOPERATIVE DIAGNOSIS: SAME

OPERATION: AORTO-FEMORAL BYPASS ON LEFT WITH STRAIGHT GRAFT DOUBLE VELOUR 8 MM. GRAFT.

PROCEDURE: With the patient on the operating table resting in decubitus supine under general satisfactory anesthesia, an arterial line on left wrist, CVP line on the right internal jugular vein was placed as well as a Foley catheter. Then the whole abdomen and lower extremities were prepped and draped in sterile fashion. Oblique incision was made in the left groin exposing the common femoral artery and dissected down until the profundus femorus artery was identified. At this area in the posterior wall, there were some atheromatous plaques in the superficial femoral artery. Then, oblique incision was made on the left lower abdomen and dividing the internal oblique aponeurosis, the internal oblique muscle and the transverse muscle and went right in the preperitoneal space. and extraperitoneally, we approached retracting to the right side of the viscus. We approached in this way the left ileac artery and we had beautiful exposure including the lower portion of the aorta. We recognized that the area of atheromatous plaques was not only on the left ileac artery but also the right as well as in the lower portion of the aorta. The ureter was identified on this side and preserved. Then, proximal and distal control was obtained in the left ileac. 5,000 units of Heparin was given IV, allowing the drug to circulate for 2 minutes and arteriotomy was done on this portion of the aorta and a side-to-side double velour Dacron graft was placed with Prolene #5-0 with continuous sutures. Then, a tunnel was made and passed to the left groin and anastomosed in the common femoral artery, right on top of the takeoff from the femoralis profunda artery. In the same fashion side-to-side with the same Prolene material, 5-0 Prolene. Then, the clamp was released and the Heparin was reversed, irrigation was done with Keflin solution in the abdominal cavity as well as in the groin. Hemostasis was achieved satisfactorily. Flow studies were done and we had flow up to 230. The abdominal incision

Signed _____ M

Name	PAUL NEWMAN	Physician	W. RIVERO, M.D.
p. No.	237 05 27 92	Room	B6
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237 05 27 92

was closed by layers using Chromic catgut for the inner layer, for the muscular layer. Tycron #2-0 for the fascia. The subcutaneous tissue was approximated with Chromic catgut and the skin with clips. In the left groin, the subcutaneous tissue was approximated with Chromic #2-0 and the skin with Prolene #3-0 with mattress sutures and continuous sutures. Sponge count was correct. The amount of blood lost was estimated at about 150 cc. No blood transfusion was given. The patient tolerated well the procedure and was sent to the CVTU in satisfactory condition.

Signed_____M

Name	PAUL NEWMAN	Physician	W. RIVERO,M.D.
( ). No.		Room	
Date Dictated	6/22/77	Type of Report	OP
Date Transcribed	6/22/77 det 1:35 pm.	☒ NGH ☐ LMH ☐ ASC	

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FIGURE 3

FIGURE 1

83-165 SAMPLE 1 X4.8

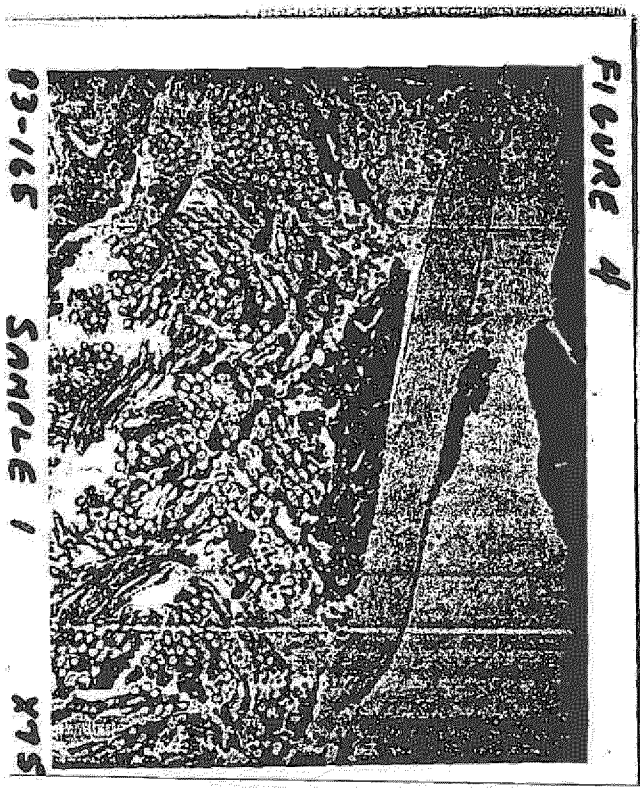


FIGURE 4

83-165 SAMPLE 1 X4.8

FIGURE 2

83-165 SAMPLE 1 X4.8

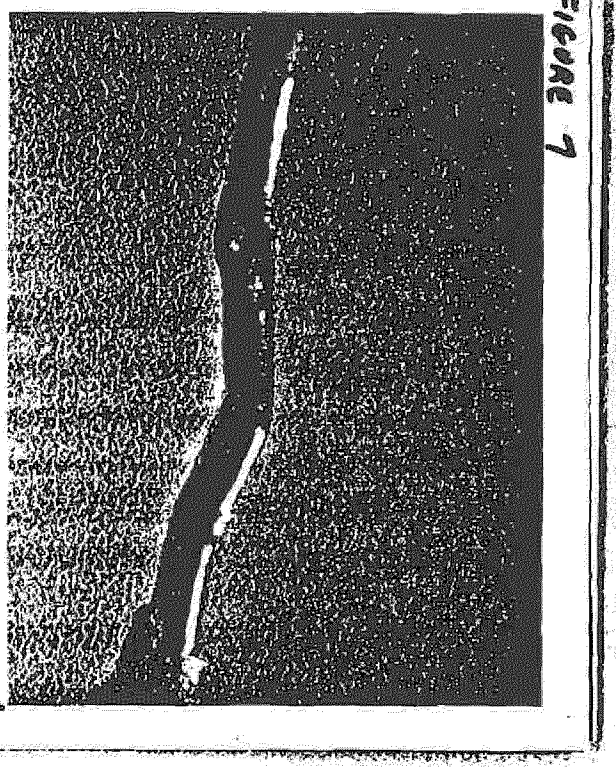


FIGURE 7
83-145 Sample 3 Comp. 2
X100

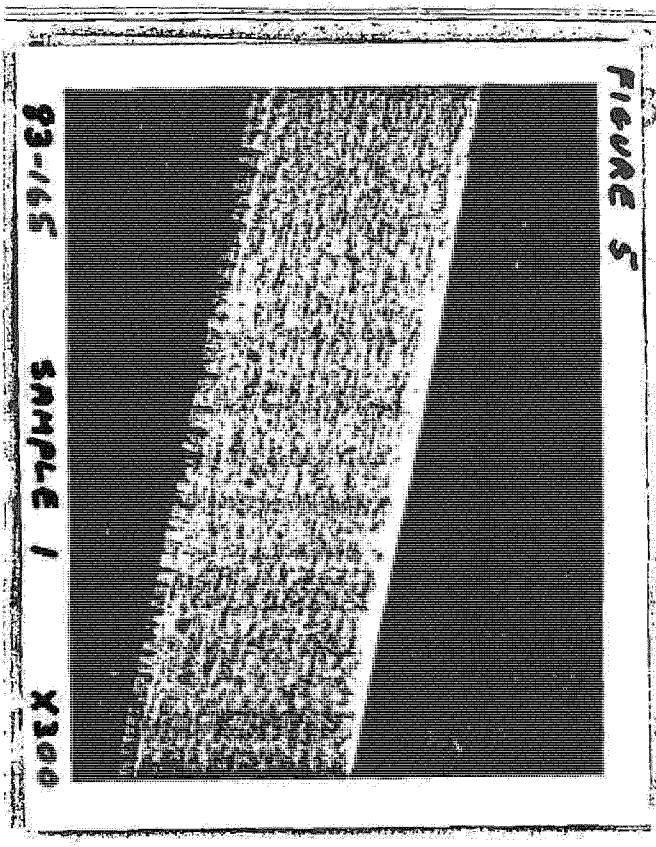


FIGURE 5
83-145 Sample 1
X100


FIGURE 8
83-145 Sample 4
X324


FIGURE 6
83-145 Sample 2
X324

855375

ETHICON

INC.

SOMERVILLE . NEW JERSEY

March 25, 1983

To: See Distribution

Subject: EXAMINATION OF 5/0 AND 6/0 CARDIOVASCULAR PROLENE* SUTURES EXPLANTED AFTER 2 TO 6 YEARS IMPLANTATION

Nine samples were submitted by the Research Foundation through Dr. Lunn. Three of these had been stored in formalin from the time of removal from the patient. The others had all been allowed to dry. Sample I.D. is listed in Results.

The samples were examined microscopically using very diffuse backlighting created by focusing our fiberoptic ringlight on a sheet of lens tissue held about 3-4 mm below the specimen.

The dry samples were examined dry (in air). The wet samples were examined mounted in the formalin in which they were stored. After examining and taking pictures of the wet samples, they were dried and reexamined mounted in air.

Results

ERF Acc. #	Size	Implant Time	State	Observations
79-220	5/0	2.5 yrs.	Dry	Very slight cracking in one small area.
80-169	5/0	2 yrs.	Wet	No cracks.
80-169	5/0	2 yrs.	Dried	Very slight cracks.
81-50	5/0	2 yrs.	Dry	No cracks, very tight flattened knot, suture surface very rough.
81-419	6/0	4 yrs.	Dry	Moderately cracked.
82-147	5/0	3 yrs.	Dry	Cracked
82-147	5/0	3 yrs.	Wet	Barely visible cracks in small area.
82-147	5/0	3 yrs.	Dried	Slight cracking plainly visible.

ERF Acc. #	Size	Implant Time	State	Observations
83-165	5/0	5.5 yrs.	Dry	Cracked
83-165	6/0	6 yrs.	Dry	Severely cracked.
83-165	6/0	6 yrs.	Wet	No Cracks
83-165	6/0	6 yrs.	Dried	Severely cracked.

General Observations & Conclusions

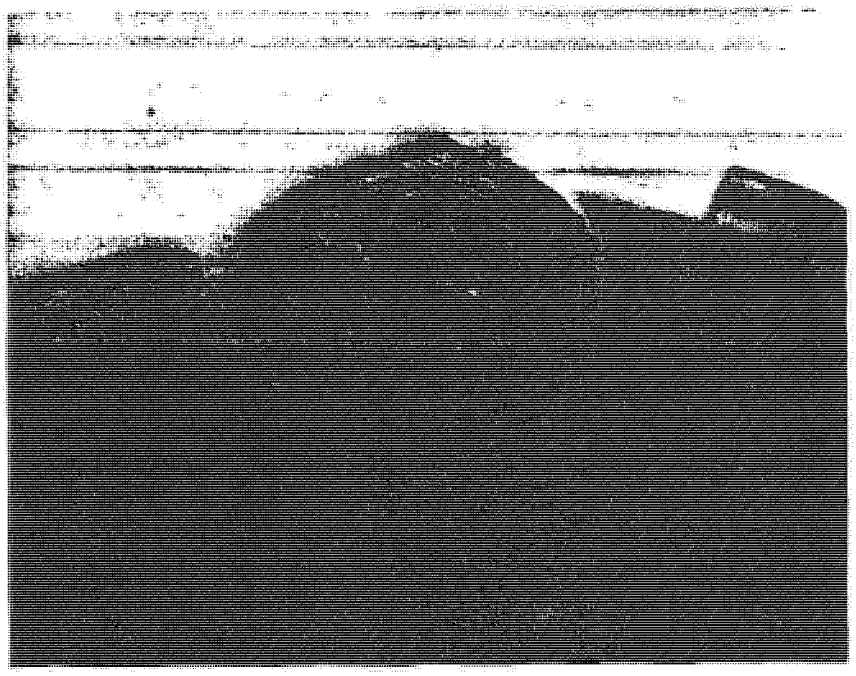
Sutures kept in the wet state do not exhibit cracks. Upon drying, cracks appear - this was actually observed happening by drying "83-165 6 yr. wet" on the microscope stage. It is obvious that the severity of cracking is related to the implantation time.

Emil Borysko, Ph.D.

sam

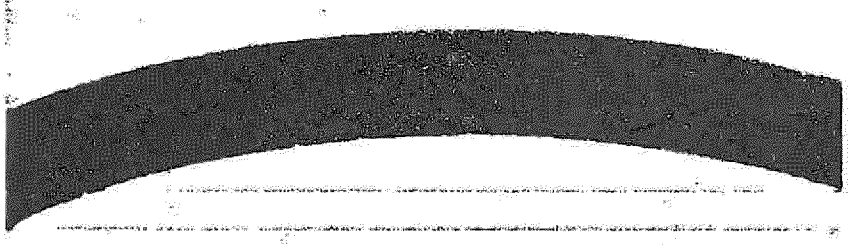
TO: Dr. A. J. Melveger
to
Dr. R. L. Kronenthal
to
Dr. A. J. Levy
to
Mr. E. A. Block
to
Dr. A. C. Lunn
to
Dr. B. Schwartz
to
Dr. J. McDivitt
to
Dr. P. Moy
to
Mr. R. Lilenfeld
to
Dr. E. Menezes

5/0 PROLENE explant 2 yr. 81-50 DRY 110X



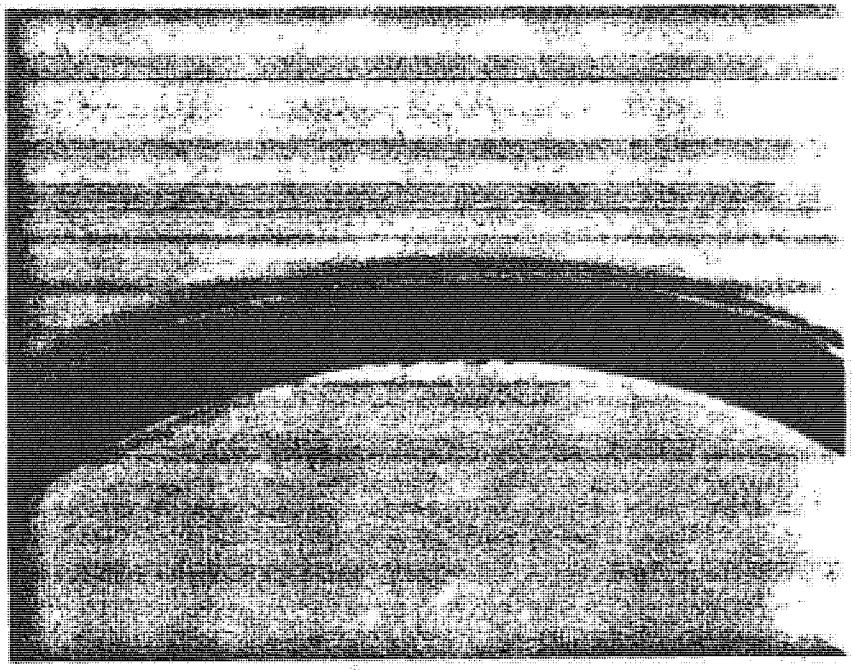
This is the only dry storage sample that did not show any sign of cracking. The knot is so tight and compressed that it is hard to believe that this is a real explant.

5/0 PROLENE explant 2 yr. 80-169 WET 110X

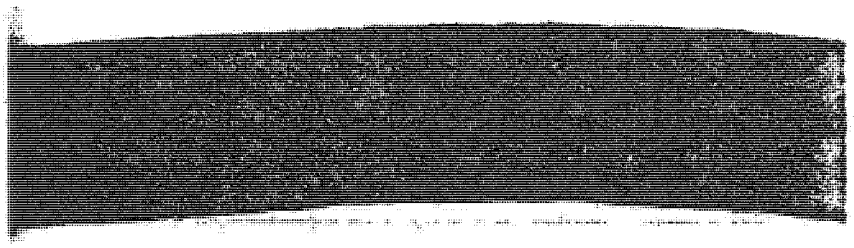


No cracks when kept in the wet state. Cracks develop upon drying under ambient conditions

5/0 PROLENE explant 2 yr. 80-169 WET/DRY 110X

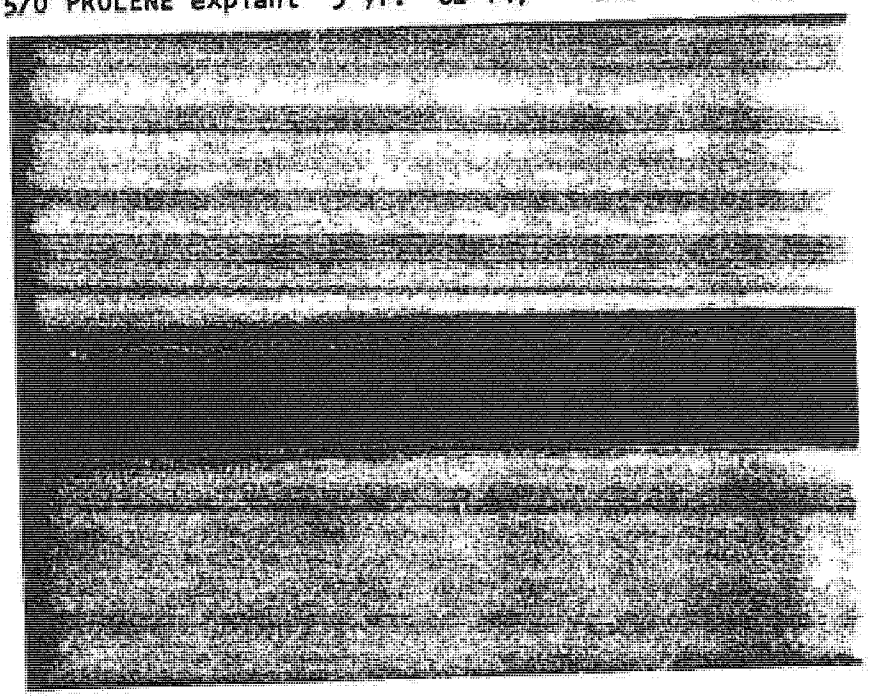


5/0 PROLENE explant 2.5 yr 79-220 DRY 110X

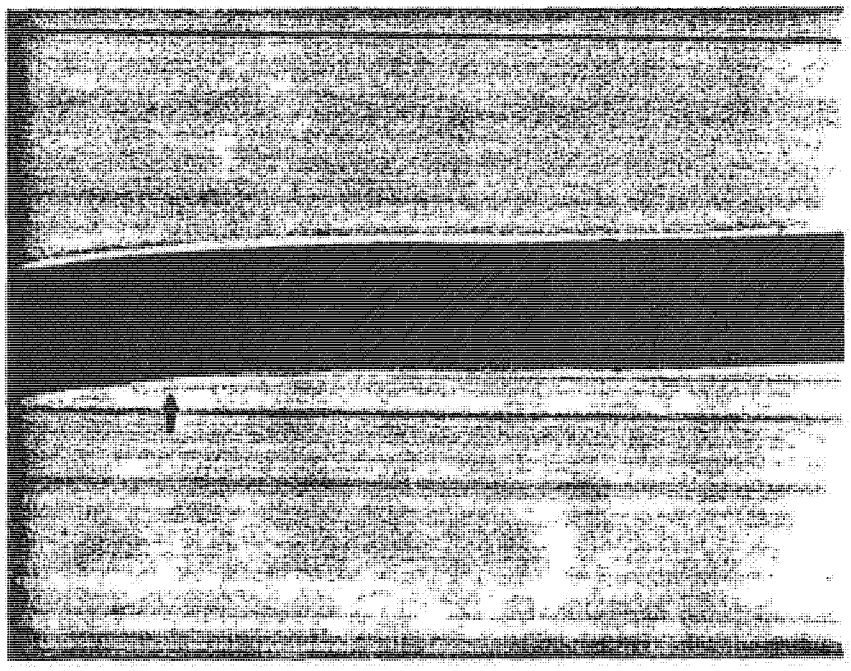


All but one of the dry storage samples exhibited surface cracks. The severity of the cracking is directly related to time the sutures were implanted.

5/0 PROLENE explant 3 yr. 82-147 DRY 110X

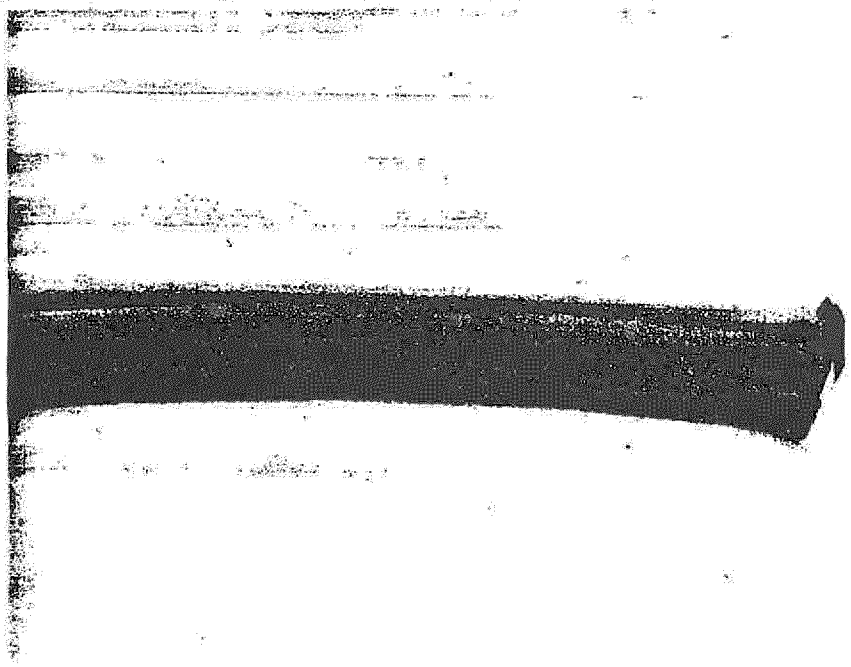


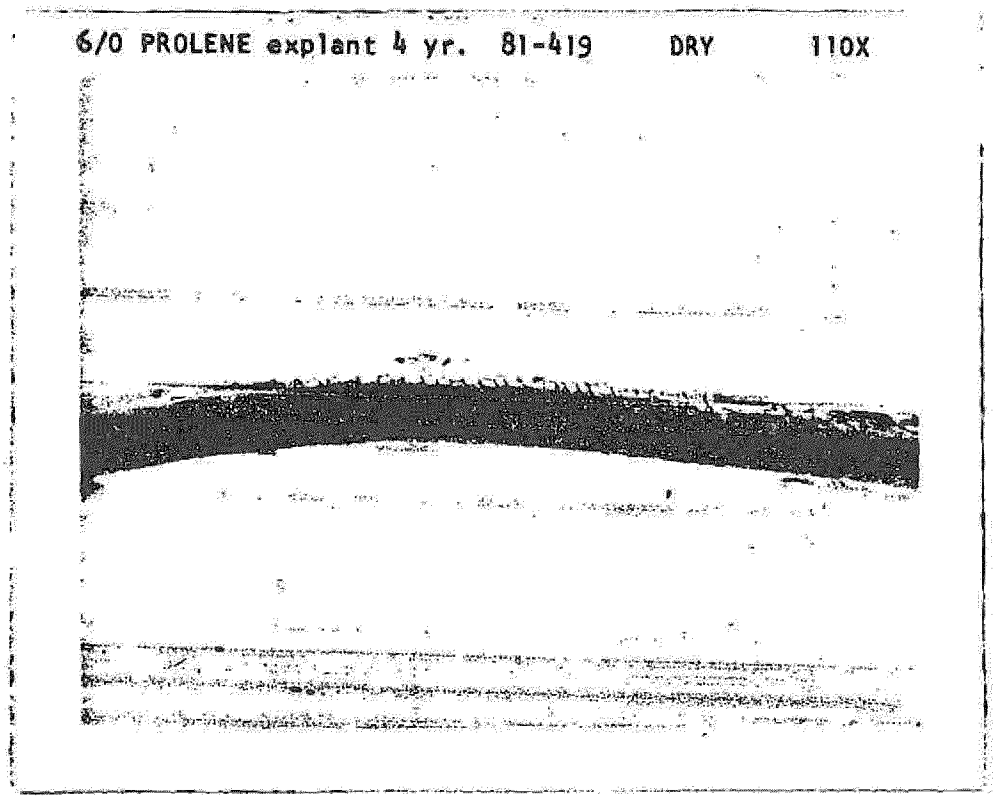
5/0 PROLENE explant 3 yr. 82-147 WET 110X



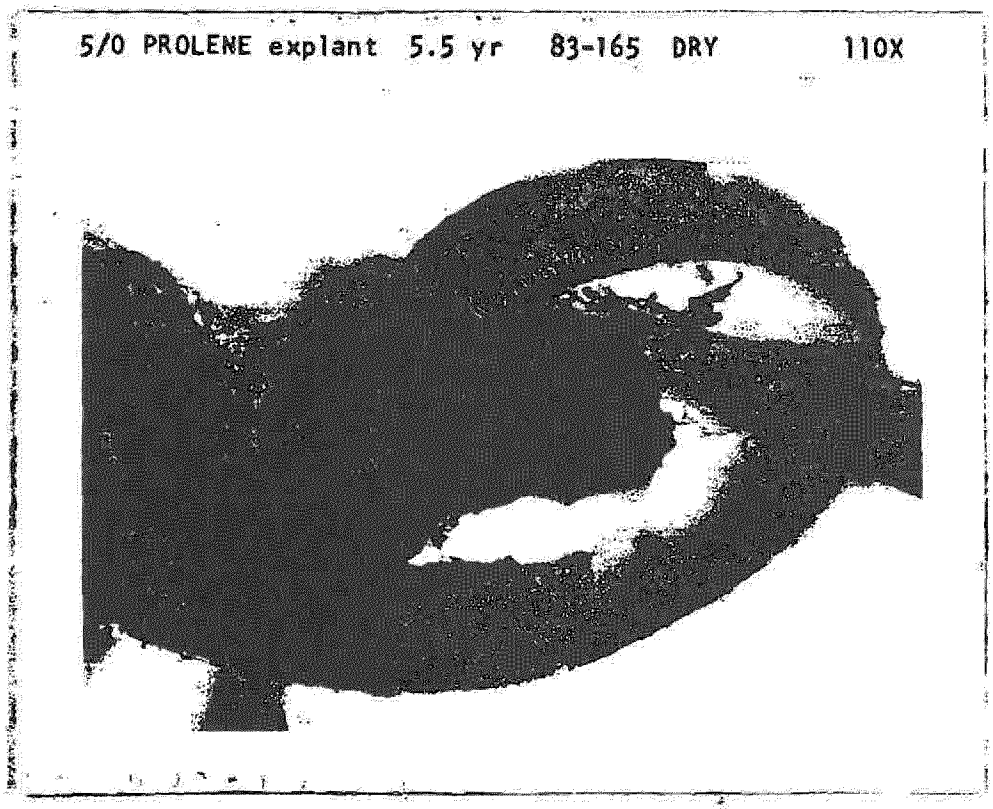
A few tiny cracks (arrow) were found in the wet filament. Many cracks appeared as a result of drying at ambient temperature (below)

5/0 PROLENE explant 3 yr. 82-147 WET/DRY 110X

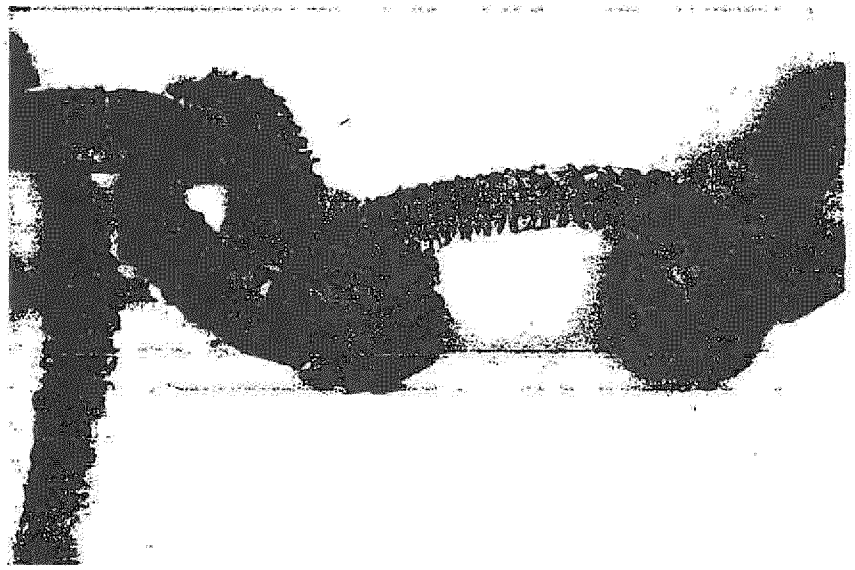




These pictures illustrate the increase in the severity of cracking with time of implantation.



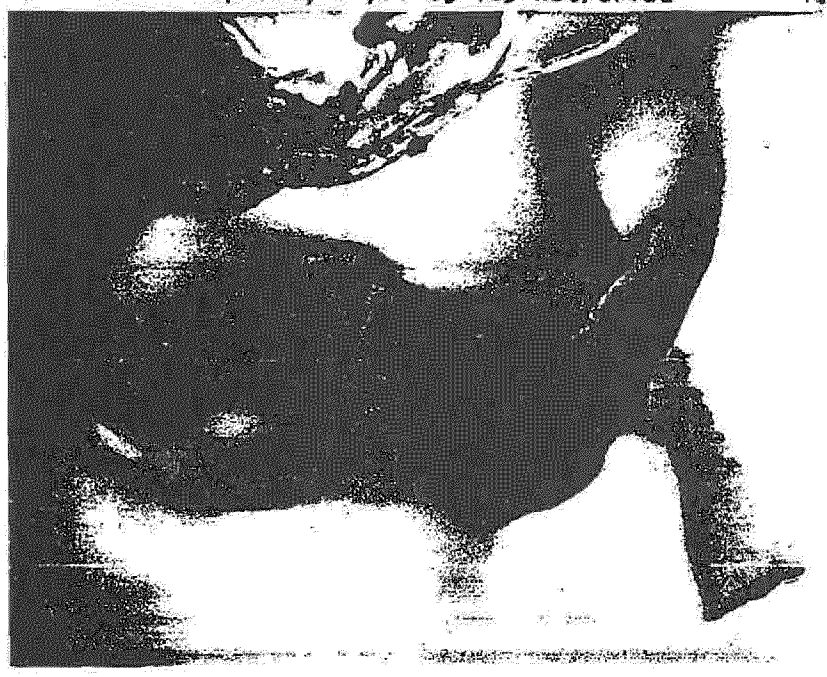
6/0 PROLENE explant, 6 yr 83-165 DRY 110X



After 6 years implantation, the suture above was explanted and allowed to dry. It shows cracks. The suture below was implanted for the same time but was never allowed to dry. It is not cracked.

6/0 PROLENE explant, 6 yr. 83-165 wet 110X

6/0 PROLENE explant, 6 yr. 83-165 wet/dried 110X



When the uncracked wet stored suture, shown in another picture, was allowed to dry, it cracked extensively as shown in these two views of the same knot. We were able to watch the suture crack as it dried on the microscope stage.

6/0 PROLENE explant, 6 yr. 83-165 wet/dried 110X

SHEET PROTECTOR PS-8

SHEET PROTECTOR PS-8

84-1162

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ETHICON
RESEARCH
FOUNDATION

SOMERVILLE, NEW JERSEY 08876

To: Dr. R. L. Kronenthal

May 2, 1984

cc: Dr. A. W. Fetter
Mr. G. G. Jones
Dr. A. J. Levy
Mr. R. Lilenfeld
Dr. D. C. Marshall
Dr. A. Melveger
Mr. R. Reinhardt
RDCF

Subject: EXAMINATION OF PROLENE* (POLYPROPYLENE) SUTURES FROM HUMAN CARDIOVASCULAR EXPLANTS

ERF ACCESSION NO.

84-194

PROJECT NO. 16104

SUMMARY

Six, formalin fixed tissue explants, containing PROLENE suture were received for evaluation of surface cracking and tensile strength measurement. Samples 1-5 were received from Dr. Margaret Bellingham, Stanford University Medical Center, and had PROLENE suture in residence from 1 year 2 months to 4 years 3 months post-op, size 3-0 and 4-0. Sample 6, size 5-0, was sent by Dr. Richard Sanders, Denver Colorado and had PROLENE in residence for 7 years.

Continuous PROLENE suture lines were carefully removed from the fixed cardiovascular specimens while keeping sutures wet. Subsequently, sutures were examined by light microscopy while wet and dry. Histological preparations of PROLENE cross-sections in tissue were stained in Phloxine and examined for cracking. Sample 1-5 showed no surface cracking in light microscopic examinations of both explanted suture or histological sections. Sample 6 displayed severe surface cracking of a 3 to 4.5 micron layer as measured in histological cross-sections.

The average breaking strength remaining for size 3-0 was 76.5% (range 47% - to 93%) and for size 4-0 was 98.25% (range 86% - 110%) when compared to similar size controls. Only one length of 5-0 PROLENE was available for tensile strength measurement indicating 76% strength remaining for the 7 year specimen.

Reported by Barbara Matlaga 5/2/84
B. Matlaga, B.S., ASCP(MT)

Approved by W. D. Sheffield 5/2/84
W. D. Sheffield, V.M.D., Ph.D.

1122E/drp

ETHICON, INC.
MAY 4 1984
RD-Central File

PURPOSE

The purpose of this study was to evaluate PROLENE suture removed from human cardiovascular explants for evidence of surface cracking.

MATERIALS

The following samples of formalin fixed cardiovascular tissues were received. Each contained multiple PROLENE suture lines.

Sample Number	Tissue Type	Years Post-Op
1	Aorta Pulmonary Artery & Right Atrium	1 year, 2 months
2	Aorta Pulmonary Artery & Right Atrium	4 years, 3 months
3	Aorta Pulmonary Artery & Right Atrium	1 year, 5 months
4	Aorta Pulmonary Artery & Right Atrium	2 years
5	Aorta Pulmonary Artery & Right Atrium	1 year, 2 months
6	Dacron Graft	7 years

Sample 1-5 were received from Dr. Margaret Bellingham, Stanford University Medical Center via Mr. Garf Jones (see attached letter Jones to Block, 10/21/83). Sample 6 was sent from Dr. Richard J. Sanders of Denver, Colorado via Mr. Ron Reinhardt (see attached letter Reinhardt to Marshall, 2/4/84).

METHODS

Each tissue specimen was removed from the formalin solution and rinsed with distilled water. Thereafter, samples remained wet. PROLENE suture was carefully dissected out of the tissue specimens and kept wet in distilled water until examinations could be performed. Pieces of tissue containing cross-sections of PROLENE suture were submitted for histological preparation and staining with 1% aqueous Phloxine solution to enhance the visualization of the cracked layer.

The surface of each strand of PROLENE suture was examined by light microscopy while wet and selected photographs were taken. The specimens were then allowed to air dry and re-examined for surface cracking. Selected photographs were taken of the appearance of identical areas in wet and dry conditions. Each specimen was then sized using a micrometer and appropriate lengths were tested on the Instron for breaking strength against similar-sized controls. The following suture lots were used as controls: size 3-0, lot no. QB2FJT, size 4-0, lot no. RH2CZN and size 5-0, lot no. MQ0287.

RESULTS

The results are listed in the table below.

Sample Number	PROLENE Suture Size	Length of Residence	Surface Cracking	Size / % Strength Remaining*
1	3-0, 4-0	1 yr., 2 mos.	no	4-0 / 106%
2	4-0	4 yr., 3 mos.	no	4-0 / 86%
3	3-0, 4-0, 5-0	1 yr., 5 mos.	no	3-0 / 75% 4-0 / 90%, 102%
4	3-0, 4-0	2 yr.	no	3-0 / 93%, 47%, 91% 4-0 / 94%, 92%, 110%
5	3-0, 4-0	1 yr., 2 mos.	no	4-0 / 106%
6	5-0	7 yr.	yes	5-0 / 76%

* Lists individual data for each strand tested against a similar sized control.

Sample 6 showed evidence of severe surface cracking by light microscopic examination. The appearance of the cracked layer was not always apparent when the specimens were examined in a wet condition but were dramatically evident in dry segments of identical areas, Figure 1 & 2. However, one sample did show evidence of a cracked layer when wet and dry, Figure 3. The cracked surface layer appeared blue when examined against a light colored background, Figure 4.

In histological sections of sample 6, a cracked surface layer measuring 3.0-4.5 microns was seen, accounting for approximately 8.5% of the total cross-sectional area. This layer was birefringent when examined under polarized light microscopy. Phloxine stain had completely penetrated the cracked layer, Figure 5, or was confined to the periphery of the surface layer, Figure 6. Particles of blue dye were evident within the cracked layer, Figure 5. There was no evidence of migration of particles from the cracked surface layer into the surrounding tissue.

DISCUSSION

In this study, it was shown that a 5-0 PROLENE suture in residence within a human vascular graft for 7 years displayed surface cracking. Other specimens of size 3-0 and 4-0 in this study from cardiovasular tissue specimens did not show surface cracking. The depth of the cracking in sample #6 was 3.0 - 4.5 microns in thickness which is consistent with other specimens, from previous samples up to 6 years post-op, ERF 84-132. This additional evidence from a 7 year specimen suggests no increase in thickness

of the cracked layer over time. The cracked layer appeared blue in gross specimens and blue dye particles were evident in histological sections of the layer. This would indicate that the layer is dyed PROLENE polymer and not an isolated protein coating on the strands.

Suture samples in this study were examined in a wet and dry condition to test the hypothesis that the cracking may be an artifact of drying. In most cases, it was difficult to visualize cracking on the surface when sutures were examined wet. This phenomenon may be related to the refractive index of the media in which the samples were examined, namely water. However, in several areas, of sample 6, cracking could be seen in both wet and dry conditions. The cracked layer was always more evident and dramatic in air dry specimens.

An average of the tensile strength measurements of samples in this study show a loss of strength for all materials tested. The breaking strength remaining for size 3-0 was 76.5%, size 4-0 98.25%, and size 5-0 76%. In some cases, however, individual samples of size 3-0 and 4-0 were stronger than control samples of identical size. All samples for breaking strength evaluation were carefully examined for surface defects prior to Instron testing. Those with obvious nicks or gouges were not tested. This breaking strength data must be viewed with caution since damage to strands during removal may have occurred despite efforts to prevent it.

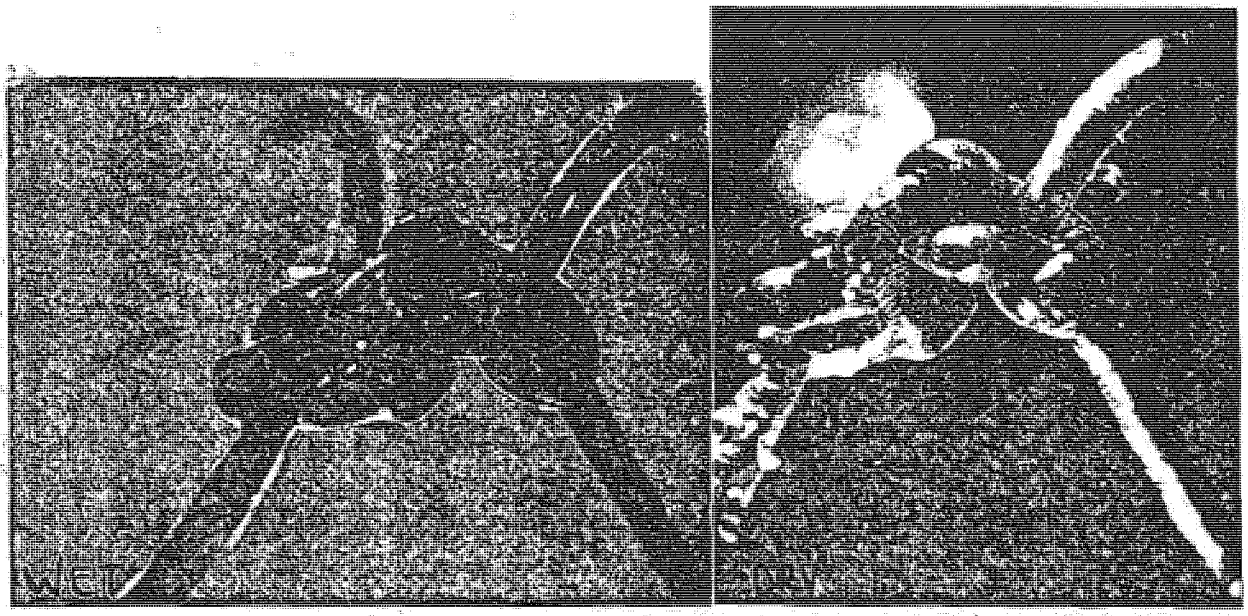


Figure 1 - Knot from sample 6 examined under wet and dry conditions. Cracking is more readily apparent in dry samples, 7 years size 5-0, magnification x40.

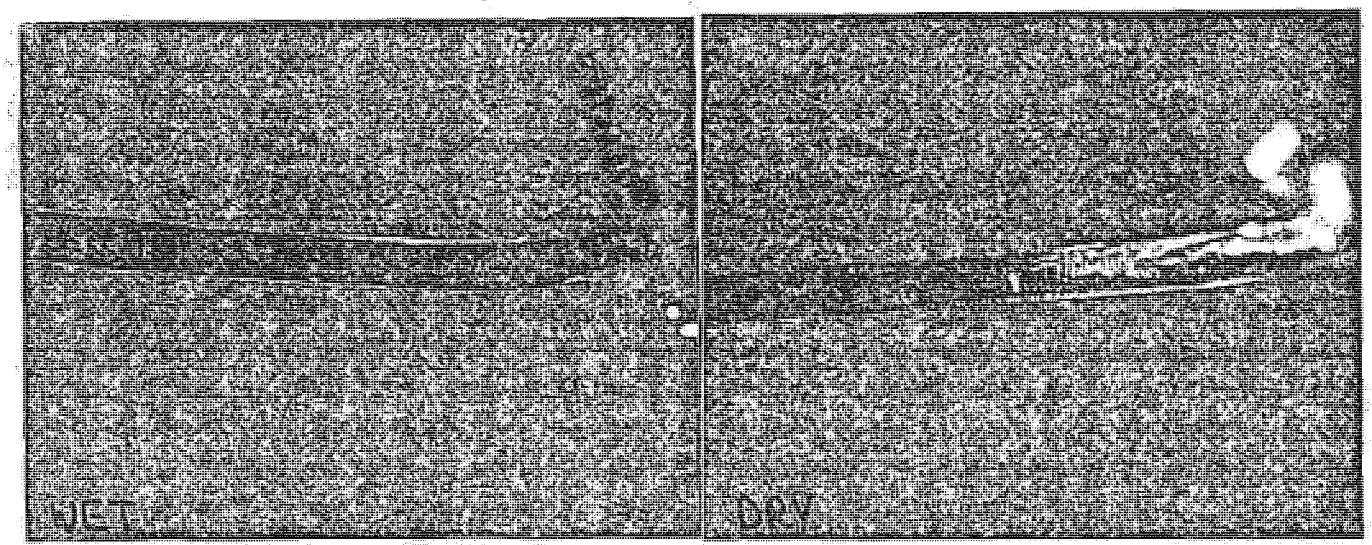


Figure 2 - Strand from sample 6 examined under wet and dry conditions. Cracking is more readily apparent in dry samples, 7 years, size 5-0, magnification X40.

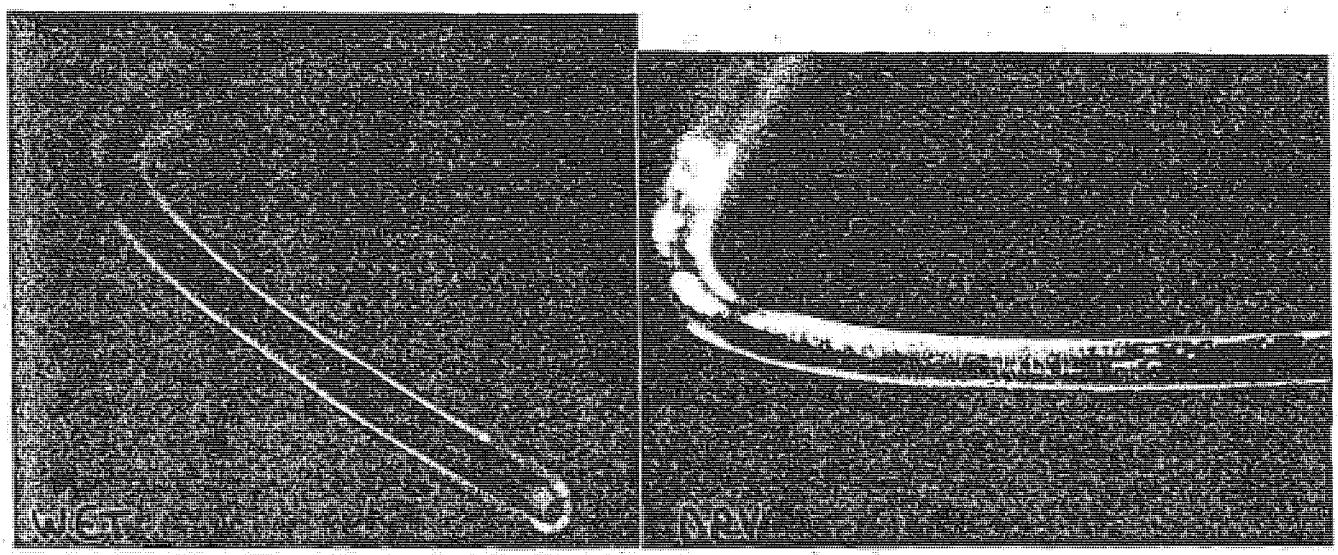


Figure 3 - Sample 6 examined under wet conditions showing some evidence of surface cracking which is more dramatic in the dry sample, 7 years, size 5-0, magnification x40.

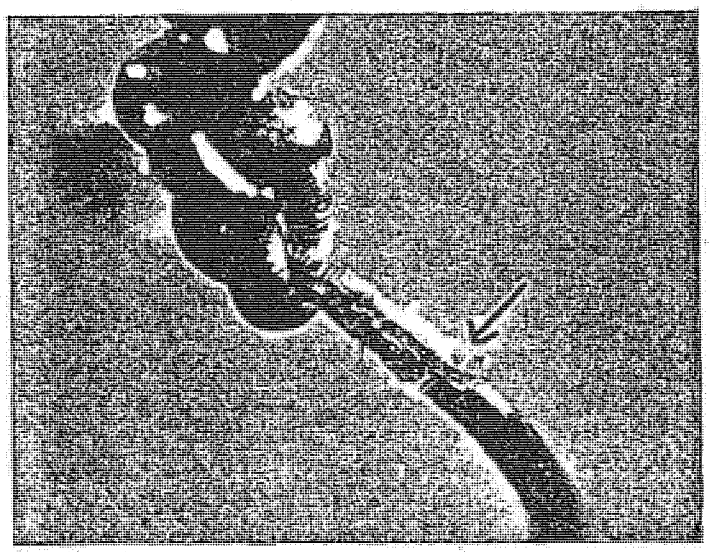


Figure 4 - Sample 6 photographed against a white background showing the blue color of the cracked surface layer, 7 years, size 5-0, magnification x40.

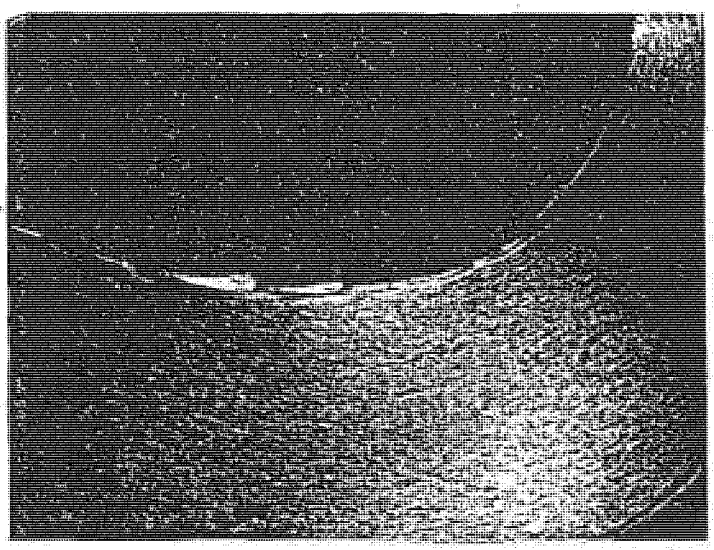


Figure 5 - Histological longitudinal sections of PROLENE from sample 6, block A, Phloxine stained. A 3.0-4.5 micron cracked surface layer is birefringent when viewed with polarized light, magnification x300.

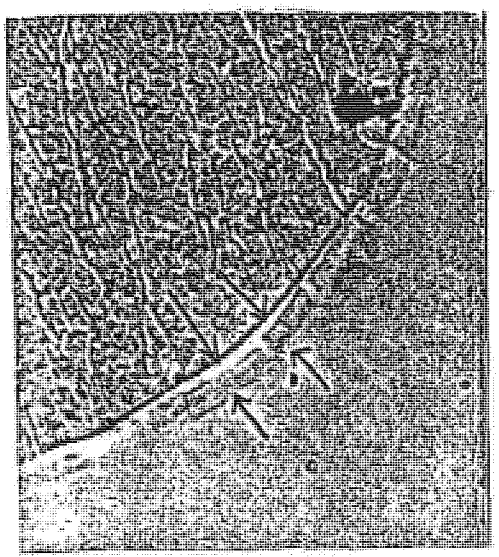


Figure 6 - Histological cross-section of sample 6, block D, Phloxine stained. Pink staining is limited to the periphery of the cracked layer in some areas. Blue dye particles can be seen within the cracked layer, magnification x1100.

ETHICON

INC.

SOMERVILLE • NEW JERSEY

February 24, 1984

To: Dr. D. C. Marshall

cc: Mr. D. M. Clapper
Mr. S. J. Czick
Mr. D. M. Lehman

Subject: PROLENE* POLYPROPYLENE SUTURE

Dave, as discussed with you, the box accompanying this memo should contain a dissected surgical specimen of a graft sutured with PROLENE suture.

This specimen was forwarded to me by Dr. Richard J. Sanders of Denver, Colorado, a General Surgery Advisory Panel member. Dr. Sanders indicated that the original procedure was performed seven years ago. The second procedure was done as the result of a suspected false aneurysm. This was not the case, as the suture line is intact.

Dr. Sanders indicated that he would be interested in writing a short paper regarding this, and would appreciate any help which we can give him (tensile strength, photographs, etc.).

I did not open the container and do not know whether any additional information is enclosed. I do know that Dr. Sanders has the complete case history, and should you have any questions regarding this, you can call him in Denver at 303/388-6461.

No. 6 7yrs.

R. J. Reinhardt

bbg
0165

Enclosure

*Trademark

Attention Suit

RICHARD J. SANDERS, M.D., P.C.
4545 E. 9th AVENUE, SUITE 250
DENVER, COLORADO 80220

Telephone
(303) 388-6461

Practice Limited To
VASCULAR SURGERY

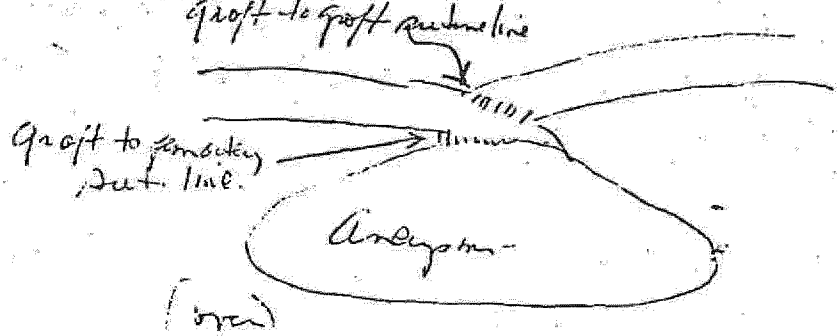
2-13-84

Ron Reinhardt
Ethicon, Inc.
Summerville, N.J. - 08876 -

Dear Ron,

The enclosed specimen is a Knitted Dacron graft - actually 2 grafts - sewn together on 1/18/77 - a little over 7 years ago. She had a true aneurysm of her Rt femoral artery which I excised on 2/9/84. I excised the 2 suture lines of the graft. -

① graft to femoral artery (aorto-femoral graft)
② graft to graft - at groin (femoro-pop. graft)



In the specimen, the suture line you can see – with intact 5-0 prolene – is the graft-to-femoral artery suture line.

The one you cannot see, is the graft-to-graft – which should have an intact 5-0 prolene suture line.

The patient is Lucile McCosta. I will be happy to write this up as a short Clinical Note on long-term evaluation of strength of prolene – 7 yrs after implantation.

Let me hear from you

Dick

Case 2:12-md-02327 Document 2555-6 Filed 08/08/16 Page 35 of 37 PageID #: 89133

ETHICON

INC.

SOMERVILLE, NEW JERSEY

October 21, 1983

To: Mr. E. A. Block cc: See Below

Subject: PROLENE* POLYPROPYLENE SUTURE/TISSUE SPECIMENS

Accompanying this memorandum are PROLENE suture explants just received from Dr. Margaret Billingham, a cardiac pathologist at Stanford University Medical Center. The attached letter from Dr. Billingham is self-explanatory.

I have made contacts to get additional tissue explants containing PROLENE suture and will transmit them to you as soon as I receive them.

G. Garfield Jones

vdh

cc: Mr. D. M. Clapper to Mr. D. r. Murray
Dr. R. L. Kronenthal to Mr. P. R. Marshall
Dr. D. C. Marshall to Dr. A. W. Fetter
Dr. A. Melveger

Enclosure

*Trademark

OCT 24 1983

STANFORD UNIVERSITY MEDICAL CENTER
300 PASTEUR DRIVE, STANFORD, CALIFORNIA 94305

Laboratory of Surgical Pathology
Room P2020 (415) 497-5252

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Roger A. Warnke, M.D., Director, Immunopathology
Margaret E. Billingham, M.D., Director, Cardiac Pathology
Robert V. Rouse, M.D.
Jon C. Ross, M.D.
Norio Azumi, M.D.

Administrative Assistant:
Leslie Culligan

Consultation Secretary:
Connie Holm
(415) 497-7482

October 14, 1983

G. Garfield Jones
Department of Clinical Research
Ethicon Inc.
Somerville, New Jersey 08876

Dear Mr. Garfield Jones:

Here at last are the samples of Prolene sutures that have been implanted in human cardiac transplant recipients. As requested, you will have the length of time the suture has been implanted, the tissue in which it resided, however, I do not know the size of the suture and hope that you will be able to determine that at Ethicon. I am sorry about the delay but I have been away and we have had some difficulty in obtaining the specimens which are used for many other research projects as you can imagine. I had not envisioned some of the difficulties which have arisen. Because of this, the number I promised you are somewhat reduced but I hope that there is enough for your study to be useful.

With best wishes.

Sincerely,

Margaret E. Billingham

Margaret E. Billingham, M.D.
Associate Professor of Pathology

MEB/rl

No 1. SPECIMEN embedded from 12/6/81 – 2/4/83 14 mo.
No 2. " " " 9/19/78 – 7/82. 4 yr. 3 mo.
No 3. " " " 11/23/81 – 9/20/83 1 yr. 5 mo.
No 4. " " " 6/29/79 · 6/28/81. 2 yr.
No 5. " " " 8/11/79 80 – 10/10/81 1 yr 2 mo

All specimens are from the aorta, pulmonary artery and right atrium - There is enough tissue left on for you to see which is which – MEB

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